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Docket No. 68811-A/JPW/GJG/MML/SK

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Sharon Cohen-Vered, et al.
Serial No. : 10/758,397
Filed : January 14, 2004
For : PARENTERAL FORMULATIONS OF PEPTIDES FOR THE
TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

1185 Avenue of the Americas
New York, New York 10036
September 10, 2004

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following documents which are listed on Form PTO-1449 (**Exhibit A**) and are also listed below.

Pursuant to the Notice appearing in the August 5, 2003 Official Gazette, because this application was filed after June 30, 2003, copies of the U.S. Patents and U.S. Patent Application Publications listed herein are not provided.

This Information Disclosure Statement is being submitted pursuant to 37 C.F.R. §1.97(b)(3) before the mailing of a first Office Action on the merits. Thus, this Information Disclosure Statement should be entered and considered. Copies of the

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documents listed below as items 6-48 are attached hereto as **Exhibits 1-41**. A copy of items 34 and 44 will be forwarded in due course.

Items 7 and 15 below were also cited in an International Search Report issued on July 18, 2002 in connection with PCT International Application No. PCT/IL02/00148, which is related to the subject application. A copy of the search report is enclosed.

1. U.S. Patent No. 5,126,249, issued June 30, 1992 to Becker et al.;
2. U.S. Patent No. 5,134,127 issued July 28, 1992, to Stella, et al.;
3. U.S. Patent No. 5,376,645 issued December 27, 1994, to Stella, et al.;
4. U.S. Patent No. 6,613,536 issued September 2, 2003, to Mozes, et al.;
5. U.S. Patent Application No. 10/758,572 filed January 14, 2004;
6. European Patent No. EP 0 495 049 B1, published July 22, 1992 (**Exhibit 1**);
7. PCT International Application Publication No. WO 96/030057 published October 3, 1996 (**Exhibit 2**);

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8. PCT International Application Publication No. WO 02/067848 published September 6, 2002 (**Exhibit 3**);
9. Audibert et al. (1981) Active antitoxic immunization by a diphtheria toxin synthetic oligopeptide. Nature, 289:593-4 (**Exhibit 4**);
10. Axelrod, O. and Mozes, E. (1986) Analysis of the biological functions and fine specificity of (T,G)-A--L specific T cell clones. Immunobiology, 172:99-109 (**Exhibit 5**);
11. Bombardier C. et al. (1992) Derivation of the SLEDAI. A disease activity index for lupus patients. The Committee on Prognosis Studies in SLE. Arthritis Rheum., 35:630-40 (**Exhibit 6**);
12. Conlon, P.J. (1983) A rapid biologic assay for the detection of interleukin 1. J. Immunol., 134:1280-2 (**Exhibit 7**);
13. Dayan M. et al. (2000) Immune response of SLE patients to peptides based on the complementarity determining regions of a pathogenic anti-DNA monoclonal antibody. J. Clin. Immunol., 20(3):187-94 (**Exhibit 8**);
14. Dean G.S. et al. (2000) Cytokines and systemic lupus erythematosus. Ann. Rheum. Dis., 59:243-51 (**Exhibit 9**);

15. Eilat, E., et al. (2000) Prevention of systemic lupus erythematosus-like disease in (NZBxNZW)F1 mice by treating with CDR1- and CDR3- based peptides of pathogenic autoantibody. J. Clin. Immunol., 20:268-78 (**Exhibit 10**);
16. Eilat, E., et al. (2001) The mechanism by which a peptide based on complementarity determining region-1 of pathogenic anti-DNA antibody ameliorates experimental SLE. Proc. Natl. Acad. Sci. U.S.A., 98: 1148-53 (**Exhibit 11**);
17. Fricke, H. et al. (1991) Idiotype specific T-cell lines inducing experimental systemic lupus erythematosus in mice. Immunology, 73:421-7 (**Exhibit 12**);
18. Fricke, H. et al. (1990) Induction of experimental systemic lupus erythematosus in mice by immunization with a monoclonal anti-La autoantibody. Int. Immunol., 2:225-30 (**Exhibit 13**);
19. Gearing, A.J.H. et al. (1994) Processing of tumor necrosis factor-alpha precursor by metalloproteinases. Nature, 370:555-7 (**Exhibit 14**);
20. Gijbels, K. et al. (1992) Gelatinase in the cerebrospinal fluid of patients with multiple sclerosis and other inflammatory neurological disorders. J. Neuroimmunol., 41:29-34 (**Exhibit 15**);
21. Goetzl, E.J. et al. (1996) Matrix metalloproteinases in immunity. J. Immunol., 156:1-4 (**Exhibit 16**);

22. Guedez, L. et al. (1996) The role of metalloproteinases and their inhibitors in hematological disorders. Crit. Rev. Oncog., 7:205-25 (**Exhibit 17**);
23. Hay, E.M. et al. (1993) The BILAG index: a reliable and valid instrument for measuring clinical disease activity in systemic lupus erythematosus. Q. J. Med., 86:447-58 (**Exhibit 18**);
24. Isenberg, D.A., et al. (1984) Anti-DNA antibody idiotypes in systemic lupus erythematosus. Lancet, 2(8400):417-22 (**Exhibit 19**);
25. Isenberg, D.A., et al. (1985) Detection of cross-reactive anti-DNA antibody idiotypes on renal tissue-bound immunoglobulins from lupus patients. J. Clin. Invest., 76(1):287-94 (**Exhibit 20**);
26. Katchalski, E. et al. (1955) Molecular weight distribution of linear and multichain polyamino acids. Statistical analysis. J. Am. Chem. Soc., 77:6175-82 (**Exhibit 21**);
27. Kotajima, L., et al., (1998) Increased levels of matrix metalloproteinase-3 in sera from patients with active lupus nephritis. Clin. Exp. Rheumatol., 16(4):409-15 (**Exhibit 22**);
28. Mendlovic, S. et al. (1988) Induction of a systemic lupus erythematosus-like disease in mice by a common human anti-DNA idiotypic. Proc. Natl. Acad. Sci. U.S.A., 85:2260-4

(**Exhibit 23**);

29. Mendlovic, S. et al. (1989) The role of anti-idiotypic antibodies in the induction of experimental systemic lupus erythematosus in mice. Eur. J. Immunol., 19:729-34 (**Exhibit 24**);
30. Mendlovic, S. et al. (1990) The genetic regulation of the induction of experimental SLE. Immunology, 69:228-36 (**Exhibit 25**);
31. Mozes, E. et al. (1989) Direct binding of a myasthenia gravis related epitope to MHC class II molecules on living murine antigen-presenting cells. EMBO J., 8:4049-52 (**Exhibit 26**);
32. Muller, G.M. et al. (1982) Anti-influenza response achieved by immunization with a synthetic conjugate. Proc. Natl. Acad. Sci. U.S.A., 79:569-73 (**Exhibit 27**);
33. Nakamura, T. et al. (1993) Gene expression of metalloproteinases and their inhibitor in renal tissue of New Zealand black/white F1 mice. Clin. Sci., 85:295-301 (**Exhibit 28**);
34. Paemen, L. et al. (1994) Evaluation of gelatinases and IL-6 in the cerebrospinal fluid of patients with optic neuritis, multiple sclerosis and other inflammatory neurological diseases. Eur. J. Neurol., 1:55-63;

35. Ruiz, P.J. et al. (1994) Induction of experimental systemic lupus erythematosus in mice by immunization with the F(ab')₂ fragment of the human anti-DNA monoclonal antibody carrying the 16/6 idiotype. Immunol. Lett., 41:79-84 (**Exhibit 29**);
36. Saren, P. et al. (1996) TNF-alpha and IL-1beta selectively induce expression of 92-kDa gelatinase by human macrophages. J. Immunol., 157:4159-65 (**Exhibit 30**);
37. Schnolzer, M. et al. (1992) In situ neutralization in Boc-chemistry solid phase synthesis. Rapid, High yield assembly of difficult sequences. Int. J. Pept. Protein Res., 40: 180-93 (**Exhibit 31**);
38. Segal, R. et al. (1997) Kinetics of cytokine production in experimental systemic lupus erythematosus: involvement of T helper cell 1/T helper cell 2-type cytokines in disease. J. Immunol., 158:3009-16 (**Exhibit 32**);
39. Shoenfeld, Y. et al. (1983) Idiotypic cross-reactions of monoclonal human lupus autoantibodies. J. Exp. Med., 158:718-30 (**Exhibit 33**);
40. Shoenfeld, Y. et al. (1982) Production of autoantibodies by human-human hybridomas. J. Clin. Invest., 70:205-8 (**Exhibit 34**);

41. Sthoeger, Z.M. et al. (1993) Monoclonal anticardiolipin antibodies derived from mice with experimental lupus erythematosus: characterization and the induction of a secondary antiphospholipid syndrome. J. Clin. Immunol., 13:127-38 (**Exhibit 35**);
42. Tan, E.M. et al. (1982) The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum., 25:1271-7 (**Exhibit 36**);
43. Theofilopoulos, A.N. et al. (1999) Tumour necrosis factor and other cytokines in murine lupus. Ann. Rheum. Dis., 58(Suppl.):149-55 (**Exhibit 37**);
44. Waisman, A. et al. (1993) The role of the 16/6 idiotype network in the induction and manifestations of systemic lupus erythematosus. Int. Immunol., 5:1293-300;
45. Waisman, A. et al. (1993) Variable region sequences of autoantibodies from mice with experimental systemic lupus erythematosus. Eur. J. Immunol., 23:1566-73 (**Exhibit 38**);
46. Waisman, A. et al. (1995) The pathogenic human monoclonal anti-DNA that induces experimental systemic lupus erythematosus in mice is encoded by a VH4 gene segment. Int. Immunol., 7:689-696 (**Exhibit 39**);

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47. Waisman, A., et al. (1997) Modulation of murine systemic lupus erythematosus with peptides based on complementarity determining regions of pathogenic anti-DNA monoclonal antibodies. Proc. Natl. Acad. Sci. U.S.A., 94(4): 4620-5 (**Exhibit 40**); and
48. Zucker, S. et al. (1999) Increased serum stromelysin-1 levels in systemic lupus erythematosus: lack of correlation with disease activity. J. Rheumatol., 26:78-80 (**Exhibit 41**).

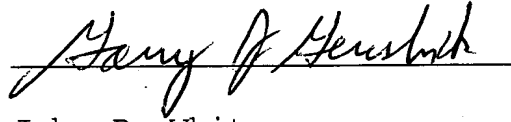
Applicants request that the Examiner review the references and make them of record in the subject application.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

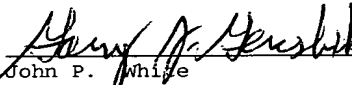

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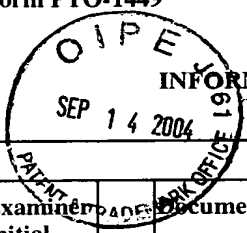
No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	
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Reg. No. 28,678 Gary J. Gershik Reg. No. 39,992	

Form PTO-1449		U.S. Department of Commerce Patent and Trademark Office		Atty. Docket No. 68811-A/JPW/GJG/JBC		Serial No. 10/758,397	
 <p align="center">INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)</p>				Applicants: Sharon Cohen-Vered et al.			
				Filing Date January 14, 2004		Group	
U.S. PATENT DOCUMENTS							
Examiner Initial	Page	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
		5 1 2 6 2 4 9	6/30/92	Becker, et al.;			
		5 1 3 4 1 2 7	7/28/92	Stella, et al.;			
		5 3 7 6 6 4 5	12/27/94	Stella, et al.;			
		6 6 1 3 5 3 6	9/2/03	Mozes, et al.;			
		10 7 5 8 5 7 2	1/14/04	Sharon Cohen-Vered, et al.			
FOREIGN PATENT DOCUMENTS							
		Document Number	Date	Country	Class	Subclass	Translation Yes No
		EPO 0 4 9 5 0 4 9	7/22/92	EPO;			
		WO 9 6 3 0 0 5 7	10/3/96	PCT;			
		02 0 6 7 8 4 8	9/6/02	WO			
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)							
		Audibert et al. (1981) Active antitoxic immunization by a diphtheria toxin synthetic oligopeptide. <u>Nature</u> , 289:593-4;					
		Axelrod, O. and Mozes, E. (1986) Analysis of the biological functions and fine specificity of (T,G)-A-L specific T cell clones. <u>Immunobiology</u> , 172:99-109;					
		Bombardier C. et al. (1992) Derivation of the SLEDAI. A disease activity index for lupus patients. The Committee on Prognosis Studies in SLE. <u>Arthritis Rheum.</u> , 35:630-40;					
		Conlon, P.J. (1983) A rapid biologic assay for the detection of interleukin 1. <u>J. Immunol.</u> , 134:1280-2;					
		Dayan M. et al. (2000) Immune response of SLE patients to peptides based on the complementarity determining regions of a pathogenic anti-DNA monoclonal antibody. <u>J. Clin. Immunol.</u> , 20(3):187-94					
		Dean G.S. et al. (2000) Cytokines and systemic lupus erythematosus. <u>Ann. Rheum. Dis.</u> , 59:243-51;					
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		Eilat, E., et al. (2001) The mechanism by which a peptide based on complementarity determining region-1 of pathogenic anti-DNA antibody ameliorates experimental SLE. <u>Proc. Natl. Acad. Sci. U.S.A.</u> , 98: 1148-53;					
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		Gearing, A.J.H. et al. (1994) Processing of tumor necrosis factor-alpha precursor by metalloproteinases. <u>Nature</u> , 370:555-7;					
		Gijbels, K. et al. (1992) Gelatinase in the cerebrospinal fluid of patients with multiple sclerosis and other inflammatory neurological disorders. <u>J. Neuroimmunol.</u> , 41:29-34;					
		Goetzl, E.J. et al. (1996) Matrix metalloproteinases in immunity. <u>J. Immunol.</u> , 156:1-4;					
		Guede, L. et al. (1996) The role of metalloproteinases and their inhibitors in hematological disorders. <u>Crit. Rev. Oncog.</u> , 7:205-25;					
EXAMINER			DATE CONSIDERED				
<p>*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>							

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 Exhibit A

